RTS-0250

<110> Brett P. Monia

Susan M. Freier

Scott Cooper

<120> ANTISENSE MODULATION OF FIBROBLAST GROWTH FACTOR RECEPTOR 2

EXPRESSION

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:	•	7
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aagt	zgact	tgc a	agcaç	gcago	cg go	cagco	gccto	c ggt	ttcct	gag	CCC	accgo	cag g	gctga	aaggca	a 180
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		-	gtc Val	-	-		-	-								342
		_	tta Leu	_		_						_				390
			caa Gln					_			_	_				438
			gag Glu		-		_	_			-				-	486
			gat Asp 75													534
			tac Tyr	_	_		_		_	_		_	_			582

RTS	-02	50					_	3-							PATENT
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					atg Met		 _				_			_	870
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		_	_	_	gtg Val	-		_	_					_	966
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					gtg Val	-	 	_	_			_	_	_	1110

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	tac ggg ccc gac ggg ctg ccc tac ctc aag gtt Tyr Gly Pro Asp Gly Leu Pro Tyr Leu Lys Val 305 310	1206
	gtt aac acc acg gac aaa gag att gag gtt ctc Val Asn Thr Thr Asp Lys Glu Ile Glu Val Leu 320 325	1254
	act ttt gag gac gct ggg gaa tat acg tgc ttg Thr Phe Glu Asp Ala Gly Glu Tyr Thr Cys Leu 335 340	1302
3 3 33	ggg ata tcc ttt cac tct gca tgg ttg aca gtt Gly Ile Ser Phe His Ser Ala Trp Leu Thr Val 350 355	1350
	aga gaa aag gag att aca gct tcc cca gac tac Arg Glu Lys Glu Ile Thr Ala Ser Pro Asp Tyr 365 370 375	1398
	tac tgc ata ggg gtc ttc tta atc gcc tgt atg Tyr Cys Ile Gly Val Phe Leu Ile Ala Cys Met 385 390	1446
	ctg tgc cga atg aag aac acg acc aag aag cca Leu Cys Arg Met Lys Asn Thr Thr Lys Lys Pro 400 405	1494
	ccg gct gtg cac aag ctg acc aaa cgt atc ccc. Pro Ala Val His Lys Leu Thr Lys Arg Ile Pro 415 420	1542
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RTS-0	250			_	5-					PATENT
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cca aa Pro Ly									_	1734
gga ga Gly Gl										1782
gac aa Asp Ly 50	s Asp					 _	 _	_	_	1830
aaa ga Lys As 520								-	_	1878
gag at Glu Me										1926
gga gc										1974
tct aaa Ser Lya										2022
atg gag Met Gli 58	ı Tyr									2070
ttc aag Phe Lys 600										2118
tac ttç Tyr Lei										2166

RTS-0250	-6-	PATENT
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	ag tgg atg gct cca gaa gcc ctg ttt gat aga gta vs Trp Met Ala Pro Glu Ala Leu Phe Asp Arg Val 670 675	2310
	gt gat gtc tgg tcc ttc ggg gtg tta atg tgg gag er Asp Val Trp Ser Phe Gly Val Leu Met Trp Glu 685 690 695	2358
	gg ggc tcg ccc tac cca ggg att ccc gtg gag gaa Ly Gly Ser Pro Tyr Pro Gly Ile Pro Val Glu Glu 00 705 710	2406
	eg aag gaa gga cac aga atg gat aag cca gcc aac eu Lys Glu Gly His Arg Met Asp Lys Pro Ala Asn 720 725	2454
	eg tac atg atg atg agg gac tgt tgg cat gca gtg eu Tyr Met Met Met Arg Asp Cys Trp His Ala Val 735 740	2502
	ea acg ttc aag cag ttg gta gaa gac ttg gat cga To Thr Phe Lys Gln Leu Val Glu Asp Leu Asp Arg 750 755	2550
	ea acc aat gag gaa tac ttg gac ctc agc caa cct ar Thr Asn Glu Glu Tyr Leu Asp Leu Ser Gln Pro 765 770 775	2598
-	ea cct agt tac cct gac aca aga agt tct tgt tct er Pro Ser Tyr Pro Asp Thr Arg Ser Ser Cys Ser 50 785 790	2646
	et gtt ttt tct cca gac ccc atg cct tac gaa cca er Val Phe Ser Pro Asp Pro Met Pro Tyr Glu Pro 800 805	2694

RTS-0250

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-7-

PATENT

RTS-0250		-8-		E	ATENT
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RTS-0250	-9-	PATENT
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RTS-0250	-10-	PATENT
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	ne Ile Cys Leu Val Leu Val Thr	
1 5	10	
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Met Ala Thr Leu Ser Leu Ala Arg		070
15 20	25 30	
13 20	25	
acc act tta gaa cca gaa gag cca (cca acc aaa tac caa atc tcc caa	744

RTS-0250

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Thr	Thr	Leu	Glu	Pro 35	Glu	Glu	Pro	Pro	Thr	Lys	Tyr	Gln	Ile	Ser 45	Gln	
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						gtg Val										840
_						aca Thr 85								_		888
		-			-	gac Asp					_	-		-	-	936
• •	_	•	•	_	_	act Thr				_			-		-	984
-					_	gat Asp		_	_		_	_		_	_	1032
_	-	-				agc Ser		_	_	_	_					1080
		_	_		_	cgg Arg 165			_	_		_	-			1128
-	_		_	_	_	gct Ala										1176
					_	gag Glu			_			_				1224
																1050

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-11-

PATENT

RTS-0250	-12-	PATENT
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	acc tac cac ctg gat gtc gtt gaa cgt tca cca cac Thr Tyr His Leu Asp Val Val Glu Arg Ser Pro His 245 250	1368
•	caa gct gga ctg cct gca aat gcc tcc acg gtg gtc Gln Ala Gly Leu Pro Ala Asn Ala Ser Thr Val Val 260 265 270	1416
Gly Gly Asp Val (gag ttt gtc tgc aag gtt tac agc gat gcc cag ccc Glu Phe Val Cys Lys Val Tyr Ser Asp Ala Gln Pro 275 280 285	1464
	atc aag cac gtg gaa aag aac ggc agt aaa aac ggg Ile Lys His Val Glu Lys Asn Gly Ser Lys Asn Gly 295 300	1512
	ccc tac ctc aag gtt ctg aaa gct gcc ggt gtt aac Pro Tyr Leu Lys Val Leu Lys Ala Ala Gly Val Asn 310 315	1560
	gag att gag gtt ctc tat att cgg aat gta act ttt Glu Ile Glu Val Leu Tyr Ile Arg Asn Val Thr Phe 325 330	1608
0 0 0 0 000	gaa tat acg tgc ttg gcg ggt aat tct atc ggg ata Glu Tyr Thr Cys Leu Ala Gly Asn Ser Ile Gly Ile 340 345 350	1656
Ser Phe His Ser	gca tgg ttg aca gtt ctg cca gcg cct gtg aga gag Ala Trp Leu Thr Val Leu Pro Ala Pro Val Arg Glu 355 360 365	1704
	gct tcc cca gat tat ctg gag ata gct att tac tgc Ala Ser Pro Asp Tyr Leu Glu Ile Ala Ile Tyr Cys 375 380	1752
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RTS-0250 -13-	PATENT
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gat aag ctg acg ctg ggc aaa ccc ctg ggg gaa ggt tgc ttc ggg caa Asp Lys Leu Thr Leu Gly Lys Pro Leu Gly Glu Gly Cys Phe Gly Gln 480 485 490	
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gcg gtc acc gtg gca gtg aag atg ttg aaa gat gat gcc aca gag aag Ala Val Thr Val Ala Val Lys Met Leu Lys Asp Asp Ala Thr Glu Lys 515 520 525	2184
gac ctg tct gat ctg gta tca gag atg gag atg atg aag atg att ggg Asp Leu Ser Asp Leu Val Ser Glu Met Glu Met Met Lys Met Ile Gly 530 535 540	
aaa cat aag aac att atc aac ctc ctg ggg gcc tgc acg cag gat gga Lys His Lys Asn Ile Ile Asn Leu Leu Gly Ala Cys Thr Gln Asp Gly 545 550 555	
cct ctc tac gtc ata gtt gaa tat gca tcg aaa ggc aac ctc cgg gaa	2328

RTS.	-025	50						-1	4-							PATENT
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											gta Val					2520
											gat Asp 650					2568
											cca Pro					2616
					Phe						cat His				Val	2664
				Val					Ile		act Thr			Gly	tca Ser	2712
			Gly					ı Glu					Let		gag Glu	
		s Arg					Thr					ı Glu			atg Met	
atg	g ato	g ag	g gat	t tga	c tgg	g cat	gct	t gta	a ccc	tca	a cag	g aga	a cco	c aca	a ttc	2856

RTS-0250	PATENT							
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-16-

RTS-0250

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PATENT

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<pre><210 > 18 <211 > 2941 <212 > DNA <213 > Homo sapiens </pre> <pre><220 > <221 > CDS <222 > (419) (2878) </pre> <pre><400 > 18 cccgcgagca aagtttggtg gaggcaacgc aagcctgagt cctttcttec tctcgttccc 60 caaatccgag ggcagccge ggggtcatg gcgtcctcc gcagcetggg gtacgegtga 120 agcccgggaga gcttggcgcc ggcgaagacc caaggaccac tcttctgcgt ttggagttgc 180 tccccgcaac cccgggctcg tcgcttctc catcccgacc cacgcggggc cggggacaac 240 acaggtcgcg gaggagcgtt gccattcaag tgactgcag agcagcgag cgcctcggt 300 cctgagccca ccgcagctga aggcattggc ggtagtccat gcccgtagag gaagtgga 360 gatgggatta acgtccacat ggagatatgg aagaggaccg gggattggta ccgtaacc 418 atg gtc agc tgg ggt cgt ttc atc tgc ctg gtc gtg gtc acc atg gca Met Val Ser Trp Gly Arg Phe Ile Cys Leu Val Val Val Thr Met Ala 1</pre>	catatgaatt t	tggggtggg gggc	acaatt cagtccatag	tagecetect cetteettee 1327	20
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RTS-0250 -69-	PATENT
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aaa gat gcc gcc gtg atc agt tgg act aag gat ggg gtg cac ttg Lys Asp Ala Ala Val Ile Ser Trp Thr Lys Asp Gly Val His Leu 65 70 75	
ccc aac aat agg aca gtg ctt att ggg gag tac ttg cag ata aagPro Asn Asn Arg Thr Val Leu Ile Gly Glu Tyr Leu Gln Ile Lys859095	_
gcc aca cct aga gac tcc ggc ctc tat gct tgt act gcc agt agg Ala Thr Pro Arg Asp Ser Gly Leu Tyr Ala Cys Thr Ala Ser Arg 100 105 110	
gta gac agt gaa act tgg tac ttc atg gtg aat gtc aca gat gcc Val Asp Ser Glu Thr Trp Tyr Phe Met Val Asn Val Thr Asp Ala 115 120 125	
tca tcc gga gat gat gag gat gac acc gat ggt gcg gaa gat ttt Ser Ser Gly Asp Asp Glu Asp Asp Thr Asp Gly Ala Glu Asp Phe 130 135 140	
agt gag aac agt aac aag aga gca cca tac tgg acc aac aca Ser Glu Asn Ser Asn Asn Lys Arg Ala Pro Tyr Trp Thr Asn Thr 145	_
aag atg gaa aag cgg ctc cat gct gtg cct gcg gcc aac act gtc Lys Met Glu Lys Arg Leu His Ala Val Pro Ala Ala Asn Thr Val 165 170 175	-
ttt cgc tgc cca gcc ggg ggg aac cca atg cca acc atg cgg tgg Phe Arg Cys Pro Ala Gly Gly Asn Pro Met Pro Thr Met Arg Trp 180 185 190	
aaa aac ggg aag gag ttt aag cag gag cat cgc att gga ggc tac Lys Asn Gly Lys Glu Phe Lys Gln Glu His Arg Ile Gly Gly Tyr 195 200 205	_
gta cga aac cag cac tgg agc ctc att atg gaa agt gtg gtc cca Val Arg Asn Gln His Trp Ser Leu Ile Met Glu Ser Val Val Pro 210 215 220	
gac aag gga aat tat acc tgt gta gtg gag aat gaa tac ggg tcc	atc 1138

RTS-0250	-70-	PATENT			
Asp Lys Gly Asn	Tyr Thr Cys Val Val Glu Asn Glu Tyr Gly Ser Ile 230 235 240				
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	gga ctg ccg gca aat gcc tcc aca gtg gtc gga gga Gly Leu Pro Ala Asn Ala Ser Thr Val Val Gly 265 270	1234			
	gtc tgc aag gtt tac agt gat gcc cag ccc cac atc Val Cys Lys Val Tyr Ser Asp Ala Gln Pro His Ile 280 285	1282			
	cac gtg gaa aag aac ggc agt aaa tac ggg ccc gac His Val Glu Lys Asn Gly Ser Lys Tyr Gly Pro Asp 295 300	1330			
	ctc aag gtt ctc aag cac tcg ggg ata aat agt tcc Leu Lys Val Leu Lys His Ser Gly Ile Asn Ser Ser 310 315 320	1378			
	ctg gct ctg ttc aat gtg acc gag gcg gat gct ggg Leu Ala Leu Phe Asn Val Thr Glu Ala Asp Ala Gly 325	1426			
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	gtc ctg cca aaa cag caa gcg cct gga aga gaa aag Val Leu Pro Lys Gln Gln Ala Pro Gly Arg Glu Lys 360 365	1522			
	tcc cca gac tac ctg gag ata gcc att tac tgc ata Ser Pro Asp Tyr Leu Glu Ile Ala Ile Tyr Cys Ile 375	1570			
	atc gcc tgt atg gtg gta aca gtc atc ctg tgc cga Ile Ala Cys Met Val Val Thr Val Ile Leu Cys Arg 390 395 400	1618			
atg aag aac acg	acc aag aag cca gac ttc agc agc cag ccg gct gtg	1666			

RTS	-02	50			•			-7			PATENT					
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	-	ctg Leu														1714
_	_	tcc Ser 435														1762
		cgc Arg														1810
		tat Tyr														1858
_	-	aca Thr														1906
_		gcg Ala														1954
		gtg Val 515														2002
		gat Asp	_				_									2050
	_	aat Asn														2098
		gtc Val		_			_									2146
ctc	cga	gcc	cgg	agg	cca	ccc	ggg	atg	gag	tac	tcc	tat	gac	att	aac	2194

PATENT

Leu	Arg	Ala	Arg 580	Arg	Pro	Pro	Gly	Met 585	Glu	Tyr	Ser	Tyr	Asp 590	Ile	Asn	
cat	at t	cct	nan	nan	cad	ato	acc	ttc	aag	gac	tta	ata	tca	tac	acc	2242
									Lys							
ALG	Vai	595	014	OI4	0211	1100	600		-2 -			605		-		
		0,0														
tac	cag	ctg	gcc	aga	cgg	atg	gag	tac	ttg	gct	tcc	caa	aaa	tgt	att	2290
Tyr	Gln	Leu	Ala	Arg	Arg	Met	Glu	Tyr	Leu	Ala	Ser	Gln	Lys	Cys	Ile	
	610					615					620					
									ttg							2338
His	Arg	Asp	Leu	Ala		Arg	Asn	Val	Leu		Thr	Glu	Asn	Asn		
625					630					635					640	
						~~~	ata	~~~	aga	ast	atc	220	aat	ata	aac	2386
									Arg							2500
Mec	гу	TIE	міа	645	FIIC	GTĀ	пси	111α	650	1100	110	11011		655	# <b>T</b> -	
				043												
tat	tac	aaa	aag	acc	acc	aat	ggg	cgg	ctt	cca	gtc	aag	tgg	atg	gct	2434
									Leu							
			660					665					670			
									act							2482
Pro	Glu	Ala	Leu	Phe	Asp	Arg		Tyr	Thr	His	Gln		Asp	Val	Trp	
		675					680					685				
				<b></b>		+~~	~~~	2+4	ttc	agt	tta	aaa	aac	taa	ccc	2530
									Phe							2330
Ser	690	Giy	Val	пеа	Mec	695	GIU	110	1110		700	0-1	0_1	~		
	050					0,00										
tac	cca	ggg	att	ccc	gtg	gag	gaa	ctt	ttt	aag	ctg	ctg	aag	gaa	gga	2578
									Phe							
705					710					715					720	
															atg	2626
His	Arg	Met	Asp	Lys	Pro	Ala	Asn	Суз	Thr		Glu	Leu	Tyr			
				725					730					735		
				<b>.</b>			- H-		+	<b>a</b> = =		999	200	++~	220	2674
															aag Lys	2074
мет	Arg	ASP	740		лт S	ATG	. val	745		GIII	. zarg	110	750		۰ ر ـــ	
			740					, <del>-1</del> J					, 50			
cao	tta	αta	gaa	. gac	tta	gat	cga	att	ctc	act	cto	aca	acc	aat	gag	2722
249	9		J = 1 G	J	- 2	_	J.									

RTS-0250	<b>-73-</b>	PATENT
Gln Leu Val Glu 755	Asp Leu Asp Arg Ile Leu Thr Leu Thr Thr Asn Glu 760 765	
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_	gag att cat gct ctt caa tgc ctc aga tcg gaa gta Glu Ile His Ala Leu Gln Cys Leu Arg Ser Glu Val 790 795 800	2818
	tcc tgt gag agc cca ttg gct gac act ggt tcc aag Ser Cys Glu Ser Pro Leu Ala Asp Thr Gly Ser Lys 805 810 815	2866
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	tggcgcc ggcgaagacc caaggaccac tettetgegt ttggagtt	
	gggeteg tegetttete catecegace caegegggge eggggaca	
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cctg	agcc	ca c	cgca	ıgctg	ja ag	gcat	tgcg	cgt	agto	cat	gccc	gtag	ag g	aagt	gtgca	360
gato	ıggat	ta a	cgtc	caca	ıt gg	gagat	atgg	aag	ıagga	ıccg	ggga	ıttgg	rta c	cgta	acc	418
_	gtc															466
Met 1	Val	Ser	Trp	Gly 5	Arg	Phe	Ile	Cys	Leu 10	Val	Val	Val	Thr	Met 15	Ala	
								++~	o ~ t	++-	~++	asa.	ast	200	202	514
	ttg															214
Thr	Leu	Ser		Ala	Arg	Pro	ser		ser	ьец	Val	GIU	30	1111	7117	
			20					25					30			
tta	gag	cca	gaa	gag	cca	cca	acc	aaa	tac	caa	atc	tct	caa	cca	gaa	562
Leu	Glu	Pro	Glu	Glu	Pro	Pro	Thr	Lys	Tyr	Gln	Ile	Ser	Gln	Pro	Glu	
		35					40					45				
gtg	tac	gtg	gct	gcg	cca	ggg	gag	tcg	cta	gag	gtg	cgc	tgc	ctg	ttg	610
	Tyr															
	50					55					60					
222	gat	מככ	acc	ata	atc	agt	t.aa	act	aaq	gat	aaa	ata	cac	ttg	ggg	658
	Asp	_														
65	1125				70		-		_	75	_				80	
	aac															706
Pro	Asn	Asn	Arg	Thr	Val	Leu	Ile	Gly	Glu	Tyr	Leu	Gln	Ile		Gly	
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gcc	aca	cct	aga	gac	tcc	ggc	ctc	tat	gct	tgt	act	gcc	agt	agg	act	754
Ala	Thr	Pro	Arg	Asp	Ser	Gly	Leu	Tyr	Ala	Cys	Thr	Ala	Ser	Arg	Thr	
			100					105					110			
ota	gac	agt	gaa	act	t.aa	tac	ttc	atq	ata	aat	gtc	aca	gat	gcc	atc	802
	Asp															
	_	115					120					125				
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	tcc Ser															850
ser		GТĀ	ASP	ASP	GIU	135	Asp	TIIT	Asp	GTĀ	140		vəħ	1110	val	
	130					133					T#0					
agt	gag	aac	agt	aac	aac	aag	aga	gca	cca	tac	tgg	acc	aac	aca	gaa	898
Ser	Glu	Asn	Ser	Asn	Asn	Lys	Arg	Ala	Pro	Tyr	Trp	Thr	Asn	Thr	Glu	

RTS-	-025	50						-7	5-							PATENT
145					150					155					160	
aag Lys																946
											acc Thr					994
											att Ile					1042
											agt Ser 220					1090
											gaa Glu					1138
										Arg	tcg Ser					1186
				Gly					Ala		aca Thr			Gly		1234
			Phe					Туг					Pro		atc Ile	1282
		ıle					Lys					Tyr			gac Asp	1330
	Lei					val					c Gly				tcc Ser 320	
															ggg Gly	

RTS-0250		-76-	PATENT
	325	330 33	5
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5 5	<del></del>	g gag ata gcc att tac tg u Glu Ile Ala Ile Tyr Cy 380	
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ū		c acc ccc atg ctg gca gg p Thr Pro Met Leu Ala Gl 460	
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RTS-0250	-77-	PATENT
500	505 510	
	gtg aag atg ttg aaa gat gat gcc aca gag aaa gac Val Lys Met Leu Lys Asp Asp Ala Thr Glu Lys Asp 520 525	2002
	gtg tca gag atg gag atg atg aag atg att ggg aaa Val Ser Glu Met Glu Met Met Lys Met Ile Gly Lys 535 540	2050
	ata aat ctt ctt gga gcc tgc aca cag gat ggg cct Ile Asn Leu Leu Gly Ala Cys Thr Gln Asp Gly Pro 550 555 560	2098
	gtt gag tat gcc tct aaa ggc aac ctc cga gaa tac Val Glu Tyr Ala Ser Lys Gly Asn Leu Arg Glu Tyr 565 570 575	2146
	agg cca ccc ggg atg gag tac tcc tat gac att aac Arg Pro Pro Gly Met Glu Tyr Ser Tyr Asp Ile Asn 585 590	2194
	gag cag atg acc ttc aag gac ttg gtg tca tgc acc Glu Gln Met Thr Phe Lys Asp Leu Val Ser Cys Thr 600 605	2242
	aga cgg atg gag tac ttg gct tcc caa aaa tgt att Arg Arg Met Glu Tyr Leu Ala Ser Gln Lys Cys Ile 615 620	2290
<b>J J</b>	gca gcc aga aat gtt ttg gta aca gaa aac aat gtg Ala Ala Arg Asn Val Leu Val Thr Glu Asn Asn Val 630 635 640	2338
	gac ttt gga ctc gcc aga gat atc aac aat ata gac Asp Phe Gly Leu Ala Arg Asp Ile Asn Asn Ile Asp 645 650 655	2386
_	acc acc aat ggg cgg ctt cca gtc aag tgg atg gct Thr Thr Asn Gly Arg Leu Pro Val Lys Trp Met Ala 665 670	2434
	ttt gat aga gta tac act cat cag agt gat gtc tgg Phe Asp Arg Val Tyr Thr His Gln Ser Asp Val Trp	2482

RTS-0250	-78-		PATENT				
675	680	685					
		act tta ggg ggc tcg ccc Thr Leu Gly Gly Ser Pro 700	2530				
	Val Glu Glu Leu Phe I	aag ctg ctg aag gaa gga Lys Leu Leu Lys Glu Gly 715 720	2578				
		aac gaa ctg tac atg atg Asn Glu Leu Tyr Met Met 735	2626				
		cag aga cca acg ttc aag Gln Arg Pro Thr Phe Lys 750	2674				
		act ctc aca acc aat gag Thr Leu Thr Thr Asn Glu 765	2722				
cct cta tcc tga aga Pro Leu Ser 770	gegttgg accetggage tg	ctggccac atcttgatct	2774				
gccatatgtg gtccaaga	at gaagtcaaca cgaagga	gaa tgaaggtgct gagggataaa	a 2834				
gttattgaca ttctagga	gc tectggatea aace		2868				
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agcccgggag gcttggcgcc ggcgaagacc caaggaccac tcttctgcgt ttggagttgc	180
tccccgcaac cccgggetcg tcgctttctc catcccgacc cacgcggggc cggggacaac	240
acaggtcgcg gaggagcgtt gccattcaag tgactgcagc agcagcgcag cgcctcggtt	300
cctgagccca ccgcagctga aggcattgcg cgtagtccat gcccgtagag gaagtgtgca	360
gatgggatta acgtccacat ggagatatgg aagaggaccg gggattggta ccgtaacc	418
atg gtc agc tgg ggt cgt ttc atc tgc ctg gtc gtg gtc acc atg gca	466
Met Val Ser Trp Gly Arg Phe Ile Cys Leu Val Val Val Thr Met Ala 1 5 10 15	
acc ttg tcc ctg gcc cgg ccc tcc ttc agt tta gtt gag gat acc aca	514
Thr Leu Ser Leu Ala Arg Pro Ser Phe Ser Leu Val Glu Asp Thr Thr 20 25 30	
tta gag cca gaa gag cca cca acc aaa tac caa atc tct caa cca gaa	562
Leu Glu Pro Glu Glu Pro Pro Thr Lys Tyr Gln Ile Ser Gln Pro Glu 35 40 45	
gtg tac gtg gct gcg cca ggg gag tcg cta gag gtg cgc tgc ctg ttg	610
Val Tyr Val Ala Ala Pro Gly Glu Ser Leu Glu Val Arg Cys Leu Leu	0.2.0
50 55 60	
aaa gat gcc gcc gtg atc agt tgg act aag gat ggg gtg cac ttg ggg	658
Lys Asp Ala Ala Val Ile Ser Trp Thr Lys Asp Gly Val His Leu Gly 65 70 75 80	
ccc aac aat agg aca gtg ctt att ggg gag tac ttg cag ata aag ggc	706
Pro Asn Asn Arg Thr Val Leu Ile Gly Glu Tyr Leu Gln Ile Lys Gly	
85 90 95 	
gcc aca cct aga gac tcc ggc ctc tat gct tgt act gcc agt agg act	754
Ala Thr Pro Arg Asp Ser Gly Leu Tyr Ala Cys Thr Ala Ser Arg Thr 100 105 110	
	000
gta gac agt gaa act tgg tac ttc atg gtg aat gtc aca gat gcc atc	802

RTS	-02!	50						-8	30-							PATENT
Val	Asp	Ser 115	Glu	Thr	Trp	Tyr	Phe 120	Met	Val	Asn	Val	Thr 125	Asp	Ala	Ile	
									gat Asp							850
_	_								cca Pro							898
									cct Pro 170							946
									atg Met							994
									cat His							1042
-									atg Met							1090
_	_								gag Glu							1138
									gag Glu 250							1186
									gcc Ala							1234
-	-		Phe					Tyr	agt Ser							1282
cag	tgg	atc	aag	cac	gtg	gaa	aag	aac	ggc	agt	aaa	tac	ggg	ccc	gac	1330

RTS-0250	-81-	PATENT
Gln Trp Ile Lys His Va	al Glu Lys Asn Gly Ser Lys Tyr Gly Pro . 295 300	Asp
	ag gtt ctc aag cac tcg ggg ata aat agt vs Val Leu Lys His Ser Gly Ile Asn Ser 10 315	
	t ctg ttc aat gtg acc gag gcg gat gct La Leu Phe Asn Val Thr Glu Ala Asp Ala 330 335	
_	cc tcc aat tat ata ggg cag gcc aac cag al Ser Asn Tyr Ile Gly Gln Ala Asn Gln 345 350	
	eu Pro Lys Gln Gln Ala Pro Gly Arg Glu 360 365	
	ca gac tac ctg gag ata gcc att tac tgc ro Asp Tyr Leu Glu Ile Ala Ile Tyr Cys 375 380	
Gly Val Phe Leu Ile A	cc tgt atg gtg gta aca gtc atc ctg tgc la Cys Met Val Val Thr Val Ile Leu Cys 395	
	ag aag cca gac ttc agc agc cag ccg gct ys Lys Pro Asp Phe Ser Ser Gln Pro Ala 410 415	
	gt atc ccc ctg cgg aga cag gta aca gtt rg Ile Pro Leu Arg Arg Gln Val Thr Val 425 430	
- ·	cc atg aac tcc aac acc ccg ctg gtg agg er Met Asn Ser Asn Thr Pro Leu Val Arg 440 445	
	ca acg gca gac acc ccc atg ctg gca ggg er Thr Ala Asp Thr Pro Met Leu Ala Gly 455 460	
tcc gag tat gaa ctt c	ca gag gac cca aaa tgg gag ttt cca aga	gat 1858

RTS-0250	-82-	PATENT
Ser Glu Tyr Glu Leu 465	Pro Glu Asp Pro Lys Trp Glu Phe Pro Arg Asp 470 475 480	
	aag ccc ctg gga gaa ggt tgc ttt ggg caa gtg Lys Pro Leu Gly Glu Gly Cys Phe Gly Gln Val 490 495	1906
	gtg gga att gac aaa gac aag ccc aag gag gcg . Val Gly Ile Asp Lys Asp Lys Pro Lys Glu Ala 505 510	1954
	aag atg ttg aaa gat gat gcc aca gag aaa gac Lys Met Leu Lys Asp Asp Ala Thr Glu Lys Asp 520 525	2002
	tca gag atg gag atg atg aag atg att ggg aaa Ser Glu Met Glu Met Met Lys Met Ile Gly Lys 535 540	2050
J	a aat ctt ctt gga gcc tgc aca cag gat ggg cct Asn Leu Leu Gly Ala Cys Thr Gln Asp Gly Pro 550 555 560	2098
	gag tat gcc tct aaa ggc aac ctc cga gaa tac Glu Tyr Ala Ser Lys Gly Asn Leu Arg Glu Tyr 570 575	2146
	g cca ccc ggg atg gag tac tcc tat gac att aac g Pro Pro Gly Met Glu Tyr Ser Tyr Asp Ile Asn 585 590	2194
	g cag atg acc ttc aag gac ttg gtg tca tgc acc a Gln Met Thr Phe Lys Asp Leu Val Ser Cys Thr 600 605	2242
	a cgg atg gag tac ttg gct tcc caa aaa tgt att g Arg Met Glu Tyr Leu Ala Ser Gln Lys Cys Ile 615 620	2290
	a gcc aga aat gtt ttg gta aca gaa aac aat gtg Ala Arg Asn Val Leu Val Thr Glu Asn Asn Val 630 635 640	2338
atg aaa ata gca gad	c ttt gga ctc gcc aga gat atc aac aat ata gac	2386

RTS-0250	-83-	PATENT
Met Lys Ile Ala	Asp Phe Gly Leu Ala Arg Asp Ile Asn Asn Ile Asp 645 650 655	
	acc acc aat ggg cgg ctt cca gtc aag tgg atg gct Thr Thr Asn Gly Arg Leu Pro Val Lys Trp Met Ala 665 670	2434
	ttt gat aga gta tac act cat cag agt gat gtc tgg Phe Asp Arg Val Tyr Thr His Gln Ser Asp Val Trp 680 685	2482
	tta atg tgg gag atc ttc act tta ggg ggc tcg ccc Leu Met Trp Glu Ile Phe Thr Leu Gly Gly Ser Pro 695 700	2530
	ccc gtg gag gaa ctt ttt aag ctg ctg aag gaa gga Pro Val Glu Glu Leu Phe Lys Leu Leu Lys Glu Gly 710 715 720	2578
	aag cca gcc aac tgc acc aac gaa ctg tac atg atg Lys Pro Ala Asn Cys Thr Asn Glu Leu Tyr Met Met 725 730 735	2626
	tgg cat gca gtg ccc tcc cag aga cca acg ttc aag Trp His Ala Val Pro Ser Gln Arg Pro Thr Phe Lys 745 750	2674
	gac ttg gat cga att ctc act ctc aca acc aat gag Asp Leu Asp Arg Ile Leu Thr Leu Thr Thr Asn Glu 760 765	2722
	ctt ccc tgt cct gac aag cac aat aaa agg tgc aaa Leu Pro Cys Pro Asp Lys His Asn Lys Arg Cys Lys 775 780	2770
	ggg gac ctc aca gag gca ggc gca gcc ggc tca tcg Gly Asp Leu Thr Glu Ala Gly Ala Ala Gly Ser Ser 790 795 800	2818
	agc aga aag cga gtg agg caa gag aaa atc agc aca Ser Arg Lys Arg Val Arg Gln Glu Lys Ile Ser Thr 805 810 815	2866
ggg taa acatcaga	aga tcaaagggca gcagctggag tcactgggtg gagaagcagt	2922

RTS-0250	-84-	PATENT
Gly		
g		2923
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agcccgggag gcttggcgcc ggcgaagacc	caaggaccac tcttctgcgt ttggagttg	gc 180
teccegeaac eeegggeteg tegetttete	catecegace caegegggge eggggacaa	ac 240
acaggtcgcg gaggagcgtt gccattcaag	g tgactgcagc agcagcgcag cgcctcggt	t 300
cctgagccca ccgcagctga aggcattgcg	g cgtagtccat gcccgtagag gaagtgtg	ca 360
gatgggatta acgtccacat ggagatatgg	g aagaggaccg gggattggta ccgtaacc	418
atg gtc agc tgg ggt cgt ttc atc Met Val Ser Trp Gly Arg Phe Ile 1 5		466
acc ttg tcc ctg gcc cgg ccc tcc Thr Leu Ser Leu Ala Arg Pro Ser 20		514
	aaa tac caa atc tct caa cca gaa Lys Tyr Gln Ile Ser Gln Pro Glu	

RTS-0250	-85-	PATENT
35	40 45	
	g cca ggg gag tcg cta gag gtg cgc tgc ctg ttg a Pro Gly Glu Ser Leu Glu Val Arg Cys Leu Leu 55 60	610
	g atc agt tgg act aag gat ggg gtg cac ttg ggg l Ile Ser Trp Thr Lys Asp Gly Val His Leu Gly 70 75 80	658
	a gtg ctt att ggg gag tac ttg cag ata aag ggc r Val Leu Ile Gly Glu Tyr Leu Gln Ile Lys Gly 5 90 95	706
	c tcc ggc ctc tat gct tgt act gcc agt agg act p Ser Gly Leu Tyr Ala Cys Thr Ala Ser Arg Thr 105 110	754
	t tgg tac ttc atg gtg aat gtc aca gat gcc atc r Trp Tyr Phe Met Val Asn Val Thr Asp Ala Ile 120 125	802
	t gag gat gac acc gat ggt gcg gaa gat ttt gtc p Glu Asp Asp Thr Asp Gly Ala Glu Asp Phe Val 135 140	850
	c aac aag aga gca cca tac tgg acc aac aca gaa n Asn Lys Arg Ala Pro Tyr Trp Thr Asn Thr Glu 150 155 160	898
	g ctc cat gct gtg cct gcg gcc aac act gtc aag g Leu His Ala Val Pro Ala Ala Asn Thr Val Lys 5 170 175	946
	c ggg ggg aac cca atg cca acc atg cgg tgg ctg a Gly Gly Asn Pro Met Pro Thr Met Arg Trp Leu 185 190	994
	g ttt aag cag gag cat cgc att gga ggc tac aag u Phe Lys Gln Glu His Arg Ile Gly Gly Tyr Lys 200 205	1042
	c tgg agc ctc att atg gaa agt gtg gtc cca tct s Trp Ser Leu Ile Met Glu Ser Val Val Pro Ser	1090

RTS-0250	-86-	PATENT
210	215 220	
	c tgt gta gtg gag aat gaa tac ggg tcc r Cys Val Val Glu Asn Glu Tyr Gly Ser 0 235	_
-	g gat gtt gtg gag cga tcg cct cac cgg u Asp Val Val Glu Arg Ser Pro His Arg 250 255	Pro
	g ccg gca aat gcc tcc aca gtg gtc gga u Pro Ala Asn Ala Ser Thr Val Val Gly 265 270	
	c aag gtt tac agt gat gcc cag ccc cac s Lys Val Tyr Ser Asp Ala Gln Pro His 280 285	
	g gaa aag aac ggc agt aaa tac ggg ccc l Glu Lys Asn Gly Ser Lys Tyr Gly Pro 295 300	
	g gtt ctc aag cac tcg ggg ata aat agt s Val Leu Lys His Ser Gly Ile Asn Ser 0 315	
	t ctg ttc aat gtg acc gag gcg gat gct a Leu Phe Asn Val Thr Glu Ala Asp Ala 330 335	
	c tcc aat tat ata ggg cag gcc aac cag l Ser Asn Tyr Ile Gly Gln Ala Asn Gln 345 350	
	g cca aaa cag caa gcg cct gga aga gaa u Pro Lys Gln Gln Ala Pro Gly Arg Glu 360 365	_
	a gac tac ctg gag ata gcc att tac tgc o Asp Tyr Leu Glu Ile Ala Ile Tyr Cys 375 380	
	c tgt atg gtg gta aca gtc atc ctg tgc a Cys Met Val Val Thr Val Ile Leu Cys	_

RTS	-02	50					-8	8 <b>7</b> -							PATENT
385				390					395					400	
				_	_		_		_	_	cag Gln	_	_		1666
											gta Val			_	1714
			-		_					_	ctg Leu 445				1762
					_	_	_			_	ctg Leu	_		_	1810
					_	-					ttt Phe		-	-	1858
						_		_		-	ttt Phe				1906
											ccc Pro	_			1954
											aca Thr 525				2002
											atg Met				2050
											cag Gln				2098
											ctc Leu				2146

RTS-0250	-88-	PATENT
	565 570 575	
	agg cca ccc ggg atg gag tac tcc tat gac att aac Arg Pro Pro Gly Met Glu Tyr Ser Tyr Asp Ile Asn 585 590	2194
	gag cag atg acc ttc aag gac ttg gtg tca tgc acc Glu Gln Met Thr Phe Lys Asp Leu Val Ser Cys Thr 600 605	2242
	aga cgg atg gag tac ttg gct tcc caa aaa tgt att Arg Arg Met Glu Tyr Leu Ala Ser Gln Lys Cys Ile 615 620	2290
	gca gcc aga aat gtt ttg gta aca gaa aac aat gtg Ala Ala Arg Asn Val Leu Val Thr Glu Asn Asn Val 630 635 640	2338
	gac ttt gga ctc gcc aga gat atc aac aat ata gac Asp Phe Gly Leu Ala Arg Asp Ile Asn Asn Ile Asp 645 650 655	2386
	acc acc aat ggg cgg ctt cca gtc aag tgg atg gct Thr Thr Asn Gly Arg Leu Pro Val Lys Trp Met Ala 665 670	2434
	ttt gat aga gta tac act cat cag agt gat gtc tgg Phe Asp Arg Val Tyr Thr His Gln Ser Asp Val Trp 680 685	2482
	tta atg tgg gag atc ttc act tta ggg ggc tcg ccc Leu Met Trp Glu Ile Phe Thr Leu Gly Gly Ser Pro 695 700	2530
	ccc gtg gag gaa ctt ttt aag ctg ctg aag gaa gga Pro Val Glu Glu Leu Phe Lys Leu Leu Lys Glu Gly 710 715 720	2578
	aag cca gcc aac tgc acc aac gaa ctg tac atg atgLys Pro Ala Asn Cys Thr Asn Glu Leu Tyr Met Met725730	2626
	tgg cat gca gtg ccc tcc cag aga cca acg ttc aag Trp His Ala Val Pro Ser Gln Arg Pro Thr Phe Lys	2674

RTS-0250	-89-	PATENT
740	745	750
cag ttg gta gaa gac ttg gat Gln Leu Val Glu Asp Leu Asp 755		
taa agccaaggat atgggaggga aa	aaaagggg aaagagtcat ggaa	agccag 2775
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ctc agt cag cct ctc gaa ccg Leu Ser Gln Pro Leu Glu Pro 20	•	
tga aataaaacgt ctctcttccc tt	ctttcagg aatacttgga cctc	agccaa 149
cctctcgaac agtattcacc tagtta	ccct gacacaagaa gttcttgt	tc ttcaggagat 209
gattctgttt tttctccaga ccccat	gcct tacgaaccat gccttcct	ca gtatccacac 269
ataaacggca gtgttaaaac atgaat	gact gigicigect g	310

-90-

PATENT

<210> 23 <211> 3025 <212> DNA <213> Homo sapiens

<220>

RTS-0250

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<222> (595)...(2643)

<400> 23

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gtc agc tgg ggt cgt ttc atc tgc ctg gtc gtg gtc acc atg gca acc

Val Ser Trp Gly Arg Phe Ile Cys Leu Val Val Val Thr Met Ala Thr

5 10 15

ttg tcc ctg gcc cgg ccc tcc ttc agt tta gtt gag gat acc aca tta 693 Leu Ser Leu Ala Arg Pro Ser Phe Ser Leu Val Glu Asp Thr Thr Leu 20 25 30

gag cca gaa gat gcc atc tca tcc gga gat gat gag gat gac acc gat

Glu Pro Glu Asp Ala Ile Ser Ser Gly Asp Asp Glu Asp Asp Thr Asp

RTS-0250	-91-	PATENT
35	40 45	
	gtc agt gag aac agt aac aac aag aga gca cca Val Ser Glu Asn Ser Asn Asn Lys Arg Ala Pro 55 60 65	789
	gaa aag atg gaa aag cgg ctc cat gct gtg cct Glu Lys Met Glu Lys Arg Leu His Ala Val Pro 75 80	837
	aag ttt cgc tgc cca gcc ggg ggg aac cca atg Lys Phe Arg Cys Pro Ala Gly Gly Asn Pro Met 90 95	885
	ctg aaa aac ggg aag gag ttt aag cag gag cat Leu Lys Asn Gly Lys Glu Phe Lys Gln Glu His 105 110	933
	aag gta cga aac cag cac tgg agc ctc att atg Lys Val Arg Asn Gln His Trp Ser Leu Ile Met 120 125	981
Glu Ser Val Val Pro S	tct gac aag gga aat tat acc tgt gtg gtg gag Ser Asp Lys Gly Asn Tyr Thr Cys Val Val Glu 135 140 145	1029
	atc aat cac acg tac cac ctg gat gtt gtg gag  Ile Asn His Thr Tyr His Leu Asp Val Val Glu  155 160	1077
	ccc atc ctc caa gcc gga ctg ccg gca aat gcc Pro Ile Leu Gln Ala Gly Leu Pro Ala Asn Ala 170 175	1125
	gga gac gta gag ttt gtc tgc aag gtt tac agt Gly Asp Val Glu Phe Val Cys Lys Val Tyr Ser 185 190	1173
	atc cag tgg atc aag cac gtg gaa aag aac ggc  Ile Gln Trp Ile Lys His Val Glu Lys Asn Gly  200 205	1221
	gac ggg ctg ccc tac ctc aag gtt ctc aag cac Asp Gly Leu Pro Tyr Leu Lys Val Leu Lys His	1269

RTS-0250		-92-		PATENT
210	215	220	225	
Ser Gly Ile Asn	· _	a gaa gtg ctg gct a Glu Val Leu Ala 235		1317
		ata tgt aag gtc Ile Cys Lys Val 250		1365
		g ctc act gtc ctg o Leu Thr Val Leu	_	1413
		aca gct tcc cca e Thr Ala Ser Pro 285		1461
		c ttc tta atc gcc l Phe Leu Ile Ala 300		1509
Thr Val Ile Leu		g aac acg acc aag s Asn Thr Thr Lys 315		1557
		g ctg acc aaa cgt s Leu Thr Lys Arg 330		1605
3 3 3 3		c tcc tcc atg aac Ser Ser Met Asn		1653
		c tct tca acg gca 1 Ser Ser Thr Ala 365	-	1701
		a ctt cca gag gac 1 Leu Pro Glu Asp 380	00 0 0	1749
		g ggc aag ccc ctg n Gly Lys Pro Leu		1797

RTS-0250	-93-	PATENT
3	395 400	
	gtc atg gcg gaa gca gtg gga att gac aaa gac a Val Met Ala Glu Ala Val Gly Ile Asp Lys Asp L 410 415	_
	gtc acc gtg gcc gtg aag atg ttg aaa gat gat g Val Thr Val Ala Val Lys Met Leu Lys Asp Asp A 425 430	
	ett tct gat ctg gtg tca gag atg gag atg atg a Leu Ser Asp Leu Val Ser Glu Met Glu Met Met L 440 445	_
	eac aag aat atc ata aat ctt ctt gga gcc tgc a His Lys Asn Ile Ile Asn Leu Leu Gly Ala Cys T 455 460 4	
Gln Asp Gly Pro L	etc tat gtc ata gtt gag tat gcc tct aaa ggc a eu Tyr Val Ile Val Glu Tyr Ala Ser Lys Gly A 475 480	
· -	etc cga gcc cgg agg cca ccc ggg atg gag tac t eu Arg Ala Arg Arg Pro Pro Gly Met Glu Tyr S 490 495	
	gt gtt cct gag gag cag atg acc ttc aag gac t arg Val Pro Glu Glu Gln Met Thr Phe Lys Asp L 505 510	-
	ac cag ctg gcc aga ggc atg gag tac ttg gct t Yr Gln Leu Ala Arg Gly Met Glu Tyr Leu Ala S 520 525	
	eat cga gat tta gca gcc aga aat gtt ttg gta a Tis Arg Asp Leu Ala Ala Arg Asn Val Leu Val T 535 540 5	
Glu Asn Asn Val M	etg aaa ata gca gac ttt gga ctc gcc aga gat a Met Lys Ile Ala Asp Phe Gly Leu Ala Arg Asp I 555 560	
	at tac aaa aag acc acc aat ggg cgg ctt cca g 'yr Tyr Lys Lys Thr Thr Asn Gly Arg Leu Pro V	

RTS-0250	-94-	PATENT
565	570 575	
	gaa gcc ctg ttt gat aga gta tac act Glu Ala Leu Phe Asp Arg Val Tyr Thr 585 590	
	ttc ggg gtg tta atg tgg gag atc ttc Phe Gly Val Leu Met Trp Glu Ile Phe 600 605	
Gly Gly Ser Pro Tyr I	cca ggg att ccc gtg gag gaa ctt ttt Pro Gly Ile Pro Val Glu Glu Leu Phe 615 620	
	aga atg gat aag cca gcc aac tgc acc Arg Met Asp Lys Pro Ala Asn Cys Thr 635	
	agg gac tgt tgg cat gca gtg ccc tcc Arg Asp Cys Trp His Ala Val Pro Ser 650 655	
	ttg gta gaa gac ttg gat cga att ccc Leu Val Glu Asp Leu Asp Arg Ile Pro 665 670	
cct tcc ctt atg agc a Pro Ser Leu Met Ser I 675	att ttt aga aaa tag tcttagccaa tgtto Ile Phe Arg Lys 680	etaaaa 2663
tgctcataag gaagggttgg	g ggaattaccc tttagacaca agctctaaga a	actctggata 2723
caacgggaac ttggatggat	t acagtetggg ectgetggge cagatgttee g	gaggggggcc 2783
cggcaagcag cctgtcttgo	c acattgcaac tgactggctt aatctacggc a	aagagtcctt 2843
cagctccgtc acagagtact	t ctccaatgtg ttatagttat ccttaaagct c	cttcaattca 2903
aggaagtgct tggcacgtt	t actettetga etggagggga ggtatgteae o	ctggatggtt 2963
gttggggaga cctcagggga	a ctgagttagg tctttggctg ctgactggtg a	atgtcgctga 3023
aa		3025

RTS-0250

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ggacaacaca ggtcgcggag gagcgttgcc attcaagtga ctgcagcagc agcggcagc	g 360
ggaranen ggeogeggag gagegeegee accodagega eegeageage ageggeage,	9 500
cctcggttcc tgagcccacc gcaggctgaa ggcattgcgc gtagtccatg cccgtagagg	g 420
January 1 grand 1 gran	,
aagtgtgcag atgggattaa cgtccacatg gagatatgga agaggaccgg ggattggtad	c 480
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Thr Thr Leu Glu Pro Glu Glu Pro Pro Thr Lys Tyr Gln Ile Ser Gln	
35 40 45	
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Pro Glu Val Tyr Val Ala Ala Pro Gly Glu Ser Leu Glu Val Arg Cys

55

60

50

-95-

RTS-0250

		_		_			aag Lys	_				721
							gag Glu 90					769
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							gtg Val					865
							gat Asp					913
		_		_	_	_	cca Pro					961
					-		cct Pro 170		_			1009
							atg Met					1057
							cat His					1105
							atg Met					1153
							gag Glu					1201

-96-

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Ser	Ile	Asn	His	Thr	Tyr	His	Leu	Asp	Val	Val	Glu	Arg	Ser	Pro	His	
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GIY	GIY	Asp	vaı		Pne	vaı	Cys	гуѕ	280	TYL	Ser	Asp	Ala	285	PLO	
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cac	atc	cad	taa	atc	aad	cac	ata	naa	aad	aac	ggc	agt	aaa	tac	aaa	1393
		_			_		_				Gly					
1110	110	0111	290		_, _	1122		295			1		300	- 1	- 4	
ccc	gac	ggg	ctg	ccc	tac	ctc	aag	gtt	ctc	aag	gtt	tcg	gct	gag	tcc	1441
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Ser	Ser	Ser	Met	Asn	Ser		Thr	Pro	Leu	Val	Arg	Ile	Thr	Thr	Arg	
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																1537
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ьеи 335	ser	ser	Thr	Ala	340	.1.111	PIO	мес	Leu	345	Gly	vai	ser	GIU	350	
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Leu	Gly	Lys	Pro	Leu	Gly	Glu	Gly	Cys	Phe	Gly	Gln	Val	Val	Met	Ala	
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-											gag					1681
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		385					390					395				
				4							<b>.</b>	<b></b>		<b>+</b> - +	~~ <del>-</del>	1700
_	-										aaa					1729
Ala		ьуs	Met	ьeu	гÀг		Asp	ALA	rnr	GIU	Lys	ASP	ьeu	ser	Asp	
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RTS-0250

Leu Val         Ser Glu Met Glu Met Met Lys Met Ile Gly Lys His Lys Asn 420         425         430           Let cata aat ctt ctt gga gcc tgc aca cag gat ggg cct ctc tat gtc Ile Ile Asn Leu Leu Gly Ala Cys Thr Gln Asp Gly Pro Leu Tyr Val 435         440         445           Let gag tat gcc tct aaa ggc aac ctc cga gaa tac ctc cga gcc Ile Val Glu Tyr Ala Ser Lys Gly Asn Leu Arg Glu Tyr Leu Arg Ala 450         460         460           Legg agg cca ccc ggg atg gag tac tcc tat gac att aac cgt gtt cct Arg Arg Pro Pro Gly Met Glu Tyr Ser Tyr Asp Ile Asn Arg Val Pro 465         470         475           Agg gag cag atg acc ttc aag gac ttg gtg tca tgc acc tac cag ctg Ilu Glu Glu Met Thr Phe Lys Asp Leu Val Ser Cys Thr Tyr Gln Leu 480         485         490           Agc agg agg cat ggg tat ggg tac ttg gtg tca aaa tgt att cat cga gat 281 agg tac ttg gct tcc caa aaa tgt att cat cga gat 281 agg tac ttg gct tcc caa aaa tgt att cat cga gat 281 agg tac ttg gct tcc caa aaa tgt att cat cga gat 281 agg tac agg aar 385 books 500         200         200         200         200         200         200         200         200         200         200         200         200         200         200         200         200         200         200         200         200         200         200         200         200         200         200         200         200         200         200         200         200         200         200         200         200																	
atc ata aat ctt ctt gga gcc tgc aca cag gat ggg cct ctc tat gtc  lie Ile Asn Leu Leu Gly Ala Cys Thr Gln Asp Gly Pro Leu Tyr Val  435  ata gtt gag tat gcc tct aaa ggc ac ctc cga gaa tac ctc cga gcc  lle Val Glu Tyr Ala Ser Lys Gly Asn Leu Arg Glu Tyr Leu Arg Ala  450  agg agg cca ccc ggg atg gag tac tcc tat gac att ac cgg gtt cct  larg Arg Pro Pro Gly Met Glu Tyr Ser Tyr Asp Ile Asn Arg Val Pro  465  agg agg acg atg acc ttc aag gac ttg gtg tca tgc acc tac cag ctg  llu Glu Gln Met Thr Phe Lys Asp Leu Val Ser Cys Thr Tyr Gln Leu  480  agg agg gcc atg gag tac ttg gtt tcc caa aaa tgt att cat cga gat  Ala Arg Gly Met Glu Tyr Leu Ala Ser Gln Lys Cys Ile His Arg Asp  500  500  500  500  500  500  500  5	_	5 5			~		_	-	_	_							17
The Ile Asn Leu Leu Gly Ala Cys Thr Gln Asp Gly Pro Leu Tyr Val 435	415					420					425					430	
Ata gtt gag tat gcc tct aaa ggc aac ctc cga gaa tac ctc cga ggc 1																	18:
The Val Glu Tyr Ala Ser Lys Gly Asn Leu Arg Glu Tyr Leu Arg Ala 450	TIE	TTE	ASII	ьеu		GIY	AIA	Cys	1111		чэр	GIY	110	БСС		Val	
A50  455  466  Agg agg cca ccc ggg atg gag tac tcc tat gac att aac cgt gtt cct Arg Arg Pro Pro Gly Met Glu Tyr Ser Tyr Asp Ile Asn Arg Val Pro 465  470  475  Agg gag cag atg acc ttc aag gac ttg gtg tca tgc acc tac cag ctg 3lu Glu Gln Met Thr Phe Lys Asp Leu Val Ser Cys Thr Tyr Gln Leu 480  485  Agg gag agg cag atg gag tac ttg gct tcc caa aaa tgt att cat cga gat 481  Ala Arg Gly Met Glu Tyr Leu Ala Ser Gln Lys Cys Ile His Arg Asp 495  500  505  510  Atta gca gcc aga aat gtt ttg gta aca gaa aac aat gtg atg aaa ata Leu Ala Ala Arg Asn Val Leu Val Thr Glu Asn Asn Val Met Lys Ile 515  520  525  Gca gac ttt gga ctc gcc aga gat atc aac aat ata gac tat tac aaa Ala Asp Phe Gly Leu Ala Arg Asp Ile Asn Asn Ile Asp Tyr Tyr Lys 530  535  540  Agg acc acc act aat ggg cgg ctt cca gtc aag tgg atg gct cca gaa gcc Lys Thr Thr Asn Gly Arg Leu Pro Val Lys Trp Met Ala Pro Glu Ala 545  545  550  565  570  Gtg tta atg tgg gag atc ttc act tta ggg ggc tcg ccc tac cca ggg 24  25  26  27  28  29  20  20  20  20  21  21  22  24  24  25  26  26  27  27  28  28  29  20  20  20  20  20  21  21  22  23  24  24  24  25  26  26  27  27  28  28  29  20  20  20  20  20  20  20  20  20																_	18
Arg Arg Pro Pro Gly Met Glu Tyr Ser Tyr Asp Ile Asn Arg Val Pro 465	Ile	Val	Glu	_	Ala	Ser	Lys	Gly		Leu	Arg	Glu	Tyr		Arg	Ala	
465 470 475  gag gag cag atg acc ttc aag gac ttg gtg tca tgc acc tac cag ctg Glu Glu Gln Met Thr Phe Lys Asp Leu Val Ser Cys Thr Tyr Gln Leu 480 485 490  gcc aga ggc atg gag tac ttg gct tcc caa aaa tgt att cat cga gat Ala Arg Gly Met Glu Tyr Leu Ala Ser Gln Lys Cys Ile His Arg Asp 495 500 505 510  tta gca gcc aga aat gtt ttg gta aca gaa aac aat gtg atg aaa ata Leu Ala Ala Arg Asn Val Leu Val Thr Glu Asn Asn Val Met Lys Ile 515 520 525  gca gac ttt gga ctc gcc aga gat atc aac aat ata gac tat tac aaa Ala Asp Phe Gly Leu Ala Arg Asp Ile Asn Asn Ile Asp Tyr Tyr Lys 530 535 540  aag acc acc aat ggg cgg ctt cca gtc aag tgg atg gct cca gaa gcc Lys Thr Thr Asn Gly Arg Leu Pro Val Lys Trp Met Ala Pro Glu Ala 545 550 565 570  gtg ttt gat agg gag atc ttc act tta ggg ggc tcg ccc tac cca ggg 42																	19
Silu   Glu   Gln   Met   Thr   Phe   Lys   Asp   Leu   Val   Ser   Cys   Thr   Tyr   Gln   Leu   480	Arg	Arg		Pro	Gly	Met	Glu	_	Ser	Tyr	Asp	Ile		Arg	Val	Pro	
480 485 490  gcc aga ggc atg gag tac ttg gct tcc caa aaa tgt att cat cga gat 2 Ala Arg Gly Met Glu Tyr Leu Ala Ser Gln Lys Cys Ile His Arg Asp 500 500 505 510  tta gca gcc aga aat gtt ttg gta aca gaa aac aat gtg atg atg aaa ata 2 Leu Ala Ala Arg Asn Val Leu Val Thr Glu Asn Asn Val Met Lys Ile 515 520 525  gca gac ttt gga ctc gcc aga gat atc aac aat ata gac tat tac aaa Ala Asp Phe Gly Leu Ala Arg Asp Ile Asn Asn Ile Asp Tyr Tyr Lys 530 535 540  aag acc acc aat ggg cgg ctt cca gtc aag tgg atg gct cca gaa gcc Lys Thr Thr Asn Gly Arg Leu Pro Val Lys Trp Met Ala Pro Glu Ala 545 550 555  ctg ttt gat aga gta tac act cat cag agt gat gtc tgg tcc ttc ggg 2 Leu Phe Asp Arg Val Tyr Thr His Gln Ser Asp Val Trp Ser Phe Gly 560 565 565 570  gtg tta atg tgg gag atc ttc act tta ggg ggc tcg ccc tac cca ggg 2 Val Leu Met Trp Glu Ile Phe Thr Leu Gly Gly Ser Pro Tyr Pro Gly	-																19
Ala Arg Gly Met Glu Tyr Leu Ala Ser Gln Lys Cys Ile His Arg Asp 500 500 505 510  tta gca gcc aga aat gtt ttg gta aca gaa aac aat gtg atg aaa ata Leu Ala Ala Arg Asn Val Leu Val Thr Glu Asn Asn Val Met Lys Ile 515 520 525  gca gac ttt gga ctc gcc aga gat atc aac aat ata gac tat tac aaa Ala Asp Phe Gly Leu Ala Arg Asp Ile Asn Asn Ile Asp Tyr Tyr Lys 530 535 540  aag acc acc aat ggg cgg ctt cca gtc aag tgg atg gct cca gaa gcc Lys Thr Thr Asn Gly Arg Leu Pro Val Lys Trp Met Ala Pro Glu Ala 545 550 555  ctg ttt gat aga gta tac act cat cag agt gat gtc tgg tcc ttc ggg Leu Phe Asp Arg Val Tyr Thr His Gln Ser Asp Val Trp Ser Phe Gly 560 565 570  gtg tta atg tgg gag atc ttc act tta ggg ggc tcg ccc tac cca ggg 245 150 150 150 150 150 150 150 150 150 15	Glu		Gln	Met	Thr	Phe		Asp	Leu	Val	Ser		Thr	Tyr	GIn	Leu	
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Leu Ala Ala Arg Asn Val Leu Val Thr Glu Asn Asn Val Met Lys Ile  515  520  525  gca gac ttt gga ctc gcc aga gat atc aac aat ata gac tat tac aaa Ala Asp Phe Gly Leu Ala Arg Asp Ile Asn Asn Ile Asp Tyr Tyr Lys  530  535  540  aag acc acc aat ggg cgg ctt cca gtc aag tgg atg gct cca gaa gcc Lys Thr Thr Asn Gly Arg Leu Pro Val Lys Trp Met Ala Pro Glu Ala  545  550  555  ctg ttt gat aga gta tac act cat cag agt gat gtc tgg tcc ttc ggg Leu Phe Asp Arg Val Tyr Thr His Gln Ser Asp Val Trp Ser Phe Gly  560  565  570  gtg tta atg tgg gag atc ttc act tta ggg ggc tcg ccc tac cca ggg Val Leu Met Trp Glu Ile Phe Thr Leu Gly Gly Ser Pro Tyr Pro Gly	Ala 495	Arg	Gly	Met	Glu		Leu	Ala	Ser	Gln		Cys	Ile	His	Arg		
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Ala Asp Phe Gly Leu Ala Arg Asp Ile Asn Asn Ile Asp Tyr Tyr Lys 530 535 540  aag acc acc aat ggg cgg ctt cca gtc aag tgg atg gct cca gaa gcc Lys Thr Thr Asn Gly Arg Leu Pro Val Lys Trp Met Ala Pro Glu Ala 545 550 555  ctg ttt gat aga gta tac act cat cag agt gat gtc tgg tcc ttc ggg Leu Phe Asp Arg Val Tyr Thr His Gln Ser Asp Val Trp Ser Phe Gly 560 555  gtg tta atg tgg gag atc ttc act tta ggg ggc tcg ccc tac cca ggg Val Leu Met Trp Glu Ile Phe Thr Leu Gly Gly Ser Pro Tyr Pro Gly	Leu	Ala	Ala	Arg		Val	Leu	Val	Thr		Asn	Asn	Val	Met		Ile	
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Lys Thr Thr Asn Gly Arg Leu Pro Val Lys Trp Met Ala Pro Glu Ala 545  ctg ttt gat aga gta tac act cat cag agt gat gtc tgg tcc ttc ggg Leu Phe Asp Arg Val Tyr Thr His Gln Ser Asp Val Trp Ser Phe Gly 560  555  gtg tta atg tgg gag atc ttc act tta ggg ggc tcg ccc tac cca ggg Val Leu Met Trp Glu Ile Phe Thr Leu Gly Gly Ser Pro Tyr Pro Gly	Ala	Asp	Phe			Ala	Arg	Asp			Asn	lie	Asp		тyr	ьуs	
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Leu Phe Asp Arg Val Tyr Thr His Gln Ser Asp Val Trp Ser Phe Gly  560 565 570  gtg tta atg tgg gag atc ttc act tta ggg ggc tcg ccc tac cca ggg Val Leu Met Trp Glu Ile Phe Thr Leu Gly Gly Ser Pro Tyr Pro Gly	Lys	Thr			Gly	Arg	Leu		Val	Lys	Trp	Met		Pro	Glu	Ala	
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-98-

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Asp Leu Ser Gln Pro Leu Glu Gln Tyr Ser Pro Ser Tyr Pro Asp Thr	
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Met Pro Tyr Glu Pro Cys Leu Pro Gln Tyr Pro His Ile Asn Gly Ser 690 695 700	
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1110	<b>0</b>							_	_							
			_				_									
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acc	atg	aca	acc	tta	tcc	cta	acc	caa	ccc	tcc	ttc	agt	tta	att	gag	698
	Met															
	15					20		J			25					
gat	acc	aca	tta	gag	cca	gaa	gag	cca	cca	acc	aaa	tac	caa	atc	tct	746
Asp	Thr	Thr	Leu	Glu	Pro	Glu	Glu	Pro	Pro	Thr	Lys	Tyr	Gln	Ile	Ser	
30					35					40					45	
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Gln	Pro	Glu	Val		Val	Ala	Ala	Pro	55 55	GIu	Ser	Leu	GIU	Va1 60	Arg	
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-	Leu															
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His	Leu	-	Pro	Asn	Asn	Arg		Val	Leu	Ile	Gly		Tyr	Leu	Gln	
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	Lys															
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_	agg															986
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_	Ala					_	_									2001
ц				130	2			_	135	-		-	_	140		
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Asp	Phe	Val	Ser	Glu	Asn	Ser	Asn	Asn	Lys	Arg	Ala	Pro	Tyr	Trp	Thr	
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	aca															1130
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Thr	Val	Lys	Phe	Arg	Cys	Pro	Ala	Gly	Gly	Asn	Pro	Met	Pro	Thr	Met	

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ggg t										1370
cac o										1418
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	_								gta Val			1802
									ttc Phe 410			1850
_									cgg Arg			1898
	_								aac Asn			1946
									acc Thr			1994
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									gaa Glu 490			2090
									aaa Lys			2138
									gat Asp		aca Thr 525	2186
									atg Met		atg Met	2234

RTS-	025	50				-1	04-					PATENT
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cga g Arg G	-											2378
gac a Asp I 590												2426
tca t Ser C												2474
aaa t Lys (												2522
aac a Asn <i>I</i>												2570
aat a Asn 1		-										2618
tgg a Trp 1	_	_										2666
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Thr Phe Lys Gln 750	Leu Val Glu A 755	Asp Leu Asp Arg 760	Ile Leu Thr Leu Th	
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Thr Asn Glu Glu	Tyr Leu Asp 1 770	Leu Ser Gln Pro 775	Leu Glu Gln Tyr Se 780	r
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Pro Ser Tyr Pro 785		Ser Ser Cys Ser 790	Ser Gly Asp Asp Se 795	r
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Val Phe Ser Pro 800		Pro Tyr Glu Pro 805	Cys Leu Pro Gln Ty 810	r
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-127-

RTS-0250

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RTS-0250

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RTS-0250

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